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Psychosocial factors, behavioral compliance and survival in urban hemodialysis patients[1]

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Background. The medical risk factors associated with increased mortality in hemodialysis (HD) patients are well known, but the psychosocial factors that may affect outcome have not been clearly defined. Psychosocial factors could affect mortality through interaction with patients' nutrition or their compliance with the dialysis prescription. We conducted a prospective, longitudinal, multicenter study of urban HD patients to determine the contribution of compliance and psychosocial factors to patient survival.

Methods. Patients were assessed using indices of social support, patient's assessments of their well-being, including illness effects (IEQ), and satisfaction with life (SWLS), the Beck Depression Inventory (BDI), serum albumin concentration, Kt/V and protein catabolic rate (PCR). Behavioral compliance was measured three ways: percent time actually dialyzed per treatment compared to prescribed time (shortening behavior); percent sessions attended (skipping behavior) and total integrated time compliance (% TCOMP). A severity index, previously demonstrated to be a mortality marker, was used to grade medical comorbidity. The type of dialyzer the patient was treated with was noted. A Cox proportional hazards model, controlling for age, medical comorbidity, albumin concentration and dialyzer type was used to assess relative mortality risk of variations in psychoscial factors and behavioral compliance.

Results. A total of 295 patients (60.8% of those eligible) agreed to participate. The mean (± SD) age of our population was 54.6 ± 14.1 year, mean PCR was 1.06 ± 0.27 g/kg/day, and mean Kt/V 1.2 ± 0.4, suggesting the patients were well nourished and adequately dialyzed. The patients' mean BDI was 11.4 ± 8.1 (in the range of mild depression). Patients' SWLS was similar to that of a group of patients without chronic illness. After a 26 month mean follow-up period, higher levels of perceived social support, improved perception of the effects of illness and increased behavioral compliance were significantly associated with decreased relative mortality risk (0.8, 0.77, and 0.79, respectively), controlled for variations in patients' age, severity of illness, serum albumin concentration and dialyzer type. Variations in depression and Kt/V were not predictors of mortality during the observation period.

Conclusions. Lower levels of social support, decreased behavioral compliance with the dialysis prescription, and increased negative perception of the effects of illness are independently associated with increased mortality in ESRD patients treated with HD. The effects are of the same order of magnitude as medical risk factors. Such effects may be attributable to a relationship between a patients' perception of social support and effects of illness and behavior, with other factors such as the provision of better medical care in patients with larger social networks. The mechanism underlying the relationship of psychosocial factors and compliance and survival, and the effect of interventions to improve perception of illness, and increase social support and compliance with the dialysis prescription in HD patients should be studied.

In chronic medical illnesses, at least two types of risk factors may effect survival: medical parameters and psychosocial strengths [1]. The medical determinants of mortality in patients with end-stage renal disease (ESRD) treated with hemodialysis (HD) are well appreciated, consisting of older age, presence of diabetes mellitus, and to a lesser extent, of comorbid conditions such as cardiovascular and cerebrovascular disease, cancer, collagen vascular disease and chronic obstructive pulmonary disease [2]. For the United States' ESRD population, African American and women patients tend to have better survival [2]. The role of nutrition [3–5] and dose of dialysis administered (Kt/V) [3–4, 6–8] in improving survival in HD patients has been increasingly appreciated. Most recently, a study has suggested the type of dialyzer used for chronic patient treatment may have an impact on patients' survival [9].

Psychosocial variables, such as extent of depression and social support, and patients' perceptions of their well-being, may also be related to outcome in patients with acute and chronic medical illness [10–13], as well as ESRD patients treated with HD [14–18]. Such factors may affect compliance with treatment regimens [19]. In patients with ESRD treated with HD, compliance is multifactorial, consisting at least of dietary restrictions and compliance with the dialysis schedule, and therefore, difficult to measure with certainty [19–22]. The relationship between compliance and mortality in HD patients has, however, also been poorly understood, partially because there has been no gold standard for measuring compliance in patients treated for ESRD [19, 21, 22]. We recently established quantitative measures to

[1] **See *Editorial* by Levy, p 285**

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assess the effect of patients' shortening and skipping treatments, compared with physicians' prescribed times, and showed that these were often unrelated to standard biochemical compliance measures used to evaluate HD patients [21, 22].

The extent of the effect of variations in patients' psychosocial status and compliance with the dialysis prescription on outcome in patients with ESRD treated with HD is currently undetermined. These issues are potentially important, since results of recent studies have prompted a controversy, suggesting that patient outcomes in the U.S. ESRD program are relatively poor given the medical status of patients, compared with results from other countries [23]. The impact of possible effects of psychosocial factors and patient compliance on survival are also important in the era of managed care contracting for three reasons. Insurers must calculate survival risks accurately, medical determinants of outcome may be less amenable to change than selected psychoscial factors, and patients may have to accept responsibility for outcomes that may be largely under their control.

To investigate the possible influence of psychosocial factors on survival, we prospectively examined the predictive power of behavioral compliance and psychosocial variables such as extent of depressive symptoms, patients' perceptions of their level of social support and well-being, after controlling for medical risk factors, in inner city patients with ESRD treated with HD.

METHODS

Patient population and demographics of the study hemodialysis units

Patient recruitment began September 1, 1992 and concluded March 31, 1996. The observation period ended September 30, 1996. George Washington University Medical Center's Ambulatory Dialysis Unit (GWUMC), Howard University Medical Center's Dialysis Unit (HUMC), and the Washington Veterans Affairs Medical Center Dialysis Unit (VAMC), all in Washington D.C., were the study sites. The population of the three units was primarily composed of African American patients. All patients enrolled in chronic ESRD HD programs at the GWUMC, HUMC and VAMC dialysis units were eligible for the study, with the exception of HIV infected patients, patients who had a psychiatric diagnosis of psychosis and patients who scored less than 23 on a mini-mental status exam [24]. Written informed consent was obtained at GWUMC and HUMC. Verbal consent was obtained prior to patients' enrollment at the VAMC. The study was approved by the institutional review boards of the three medical centers. Details regarding our recruitment procedures have been previously reported [21]. Questionnaires were administered in an interview format by trained personnel to patients enrolled in the study. Psychosocial variables were assessed in patients at study entry, and at six month intervals thereafter. The demographics of our patient population are delineated in Tables 1 and 2.

Table 1. Demographics of hemodialysis sample

Site	*N*	Male	Female	White	African American	Hispanic	Other
GWU	93	58	35	11	77	2	3
HUH	111	61	50	3	106	1	1
VAMC	91	90	3	5	83	1	2
Total	295	209	88	19	266	4	6

Abbreviations are in the Appendix.

Table 2. Clinical medical and psychosocial characteristics of the study population ($N = 295$)

	Mean	SD	Range
Age, *years*	54.6	14.13	19–84
Diabetes, *%*	42.3	—	—
Albumin, *g/dl*	3.82	0.49	2.0–5.7
Kt/V	1.2	0.4	0.36–1.96
PCR, *g/kg/day*	1.06	0.27	0.49–2.37
MAC, *cm*	30.2	5.9	15.9–55.7
BDI	11.4	8.1	0–47
MSP	22.1	4.5	5.7–28
IEQ	64.4	26.3	6–140
SWLS	21.7	7.9	5–35
Time compliance *%*	97.8	2.9	83.3–100
Attendance *%*	98.3	6.1	38.8–100
Total time compliance *%*	95.9	7.0	36.4–100

Abbreviations are: PCR, protein catabolic rate; MAC, mean arm circumference; BDI, Beck Depression Inventory; MSP, Multidimensional Scale of Perceived Social Support; SWLS, Satisfaction with Life Scale; Time compliance, shortening behavior; Attendance, skipping behavior; Total time compliance, integrated shortening and skipping behavior.

MEASURES

Medical risk factors

Comorbidity. Disease severity (age and the presence of comorbid conditions such as cardiovascular and cerebrovascular disease, diabetes mellitus, collagen vascular disease, malignancy and the type of renal disease) was quantified by the ESRD severity coefficient [15, 25, 26], previously validated in a large sample of ESRD patients [25]. The product of age and the relative risk of additional medical illness, including diabetes mellitus, was used to derive the coefficient [25], an overall measure of the level of severity of the patient's renal and comorbid chronic illnesses.

Nutritional and dialytic parameters. These included protein catabolic rate (PCR) and Kt/V, calculated monthly at GWUMC and HUMC, and quarterly at VAMC using the percent urea reduction, as outlined by Jindal et al [27]. The dialyzer used to treat each patient at study entry was noted and categorized as (*1*) unmodified cellulose (Group 1) or (*2*) modified cellulose or synthetic (Group 2) [9]. The mean of three sequential monthly serum albumin concentrations after enrollment was determined. Mid-arm circumference

(MAC) and arm muscle area (AMA) measurements were obtained by trained personnel at study entry, as previously described [21, 28, 29].

Psychosocial variables

Depression. The Beck Depression Inventory (BDI) was used to measure depressive symptoms [30]. The BDI is a well-validated measure of depression, correlating with diagnostic criteria for depression [30], and has been used frequently to assess depression in patients with ESRD [14, 15, 21, 26, 31]. A second measure, the Cognitive Depression Index (CDI), was composed of 15 of the 21 items of the BDI [14, 15, 26]. The CDI focuses on thoughts and feelings related to the diagnosis of depression, such as guilt, disappointment and failure, and excludes somatic items [14, 26]. The CDI has previously been highly correlated with the BDI and mortality in ESRD patients [14, 15, 21, 26].

Social support. Social support is multidimensional information related to an individual as a member of a complex network in which one can give and receive affection, aid, and obligation [10, 32–36]. The Multidimensional Scale of Perceived Social Support (MSP) [35] is a 12 item inventory that assesses overall perceived social support from special persons, family and friends. A special person is someone who may serve a special multi-support role but may not be a family member or friend, such as a clergyman, health care worker, coworker, or confidant. Each of these sources of support are factorially independent [35]. The MSP scale has demonstrated good internal and test-retest reliability [35]. The mean of the three factor scores reported by a patient were added to obtain a total social support score (MSPTOT), as used by our group previously [21, 36].

Well-being measures

Perception of illness effects. The Illness Effects Questionnaire [37, 38] is a 20 item, seven point Likert scale that assesses the individual's perception of how the illness interferes with or modifies personal and social behavior. Questions range from perceived family and personal disruption to physical problems and fears about the consequences of illness. The IEQ has an internal reliability of $\alpha = 0.93$, and a test-retest reliability of 0.99, and has been used in patients with ESRD [15, 21, 26, 32, 36]. Higher scores indicate greater levels of perceived life disruption from illness. The IEQ has previously been highly correlated with the BDI and the CDI [15, 21, 26, 36].

Quality of life. The Satisfaction with Life Scale (SWLS) is a five item scale with a 1 to 7 (low to high) satisfaction rating for each item [39, 40]. The items ask about ideal life, conditions of life and satisfaction with present and past life. Diener et al reported good internal reliablity, two month test-retest reliability and moderate correlations with a large number of subjective well-being scales, and lack of correlation with social desirability [39]. The SWLS has been used as a general global, subjective quality of life measure, as previously reported in patients treated with HD [36].

Behavioral compliance

Patients' behavioral compliance with their prescribed HD regimen was assessed using three scales, as previously described [21]: (*1*) Percent Time Compliance (% COMP) measured the amount of time the patient was actually dialyzed compared to the time physicians prescribed, only for sessions attended by the patient. This quantifies the amount of time patients decrease the length of dialysis sessions, characterizing "shortening" behavior. (*2*) Percent Attendance (% ATTEND) comprised the number of sessions attended compared to the number prescribed, quantifying the percentage of sessions from which the patient was absent without excuse (such as being hospitalized or receiving treatment as a transient patient in another unit), characterizing "skipping" behavior. (*3*) Total Time Compliance (% TCOMP) reflects the percent time the patient received dialysis compared to the total time prescribed in both attended and unattended sessions, an overall measure of compliance with the dialysis prescription, including "skipping" and "shortening" behaviors. The resulting values were averaged over a three month period, beginning with the date of study entry. Individual behavior compliance measures are highly stable over time [21].

Statistical methods

Correlations between psychosocial variables and age, medical risk factors, including demographic data, and behavioral compliance levels were assessed using Spearman Rank Order coefficients, as previously described [21, 36], because the behavioral compliance measures all displayed skewed distributions. Stability of psychosocial variables was assessed by correlating individuals' values at baseline, six month and at one year follow-up, as previously described [21]. Differences between groups were assessed by unpaired *t*-tests, chi-square analysis and analysis of variance as appropriate.

Survival time for each individual patient was determined both by the number of days between first dialysis and the end of the study observation period, or date of death, and initial study evaluation and the end of the study observation period or date of death. Survival status was confirmed using the Health Care Finance Administration data base, obtained through ESRD Network 5 (Richmond, Virginia) for all patients enrolled in the study. Cox proportional hazards regression was used to predict mortality hazard [41]. A separate equation was calculated for each medical and demographic predictor (age at time of entry into the study, gender, severity coefficent, serum albumin concentration, dialyzer type, and Kt/V).

Following the results of these initial bivariate Cox regressions, regression analyses were performed in which the relationship between compliance indicators, psychosocial

and well-being variables, and survival were examined while simultaneously controlling for the effects of variation in levels of medical risk factors, specifically patients' age, severity coefficient, level of serum albumin concentration and dialyzer type. Relative risks or hazards represent the expected change in mortality risk associated with a one SD increase in the predictor variable, except for dialyzer type and gender, or as otherwise noted. This allows for comparison of the effects of changes in levels of several risk factors across different parameters in a population [42]. Analyses were performed using PROC PHREG in SAS 6.11 (SAS Institue Inc., Cary, NC, USA). The alpha level of tests of survival and group differences was 0.05. Data are presented as mean ± SD.

RESULTS

Demographics

The total enrolled sample surveyed comprised 295 subjects, a 60.8% overall enrollment rate. Mean and median follow-up times were 26.4 ± 12.8 and 27.7 months, respectively. Nearly all (90.2%) of our patient population was comprised of African Americans (Table 1); 29.8% of the patients were female, and 42.3% had diabetes mellitus.

Medical risk factors

The mean age of our patient population was 54.6 ± 14.1 years old (Table 2). Patients had been treated with hemodialysis for mean and median times of 56.6 ± 51.9 and 41.5 months, respectively. The patients' mean PCR was 1.06 ± 0.27 g/kg/day and mean Kt/V was 1.2 ± 0.4. The mean serum albumin concentration in our patient population was 3.82 ± 0.49 g/dl. Anthropometric evaluations were performed in two hundred forty-seven of the subjects (83.7%). Anthropometry could not be performed in 48 subjects, because of disability associated with cerebrovascular disease, refusals, transfers from the unit, or because of death before assessment. The patients' mean arm circumference was 30.2 ± 5.9 cm. These findings suggest the patients were well-nourished (compared with a normative cohort of patients with ESRD treated with HD [43]) and delivery of dialysis (Kt/V) was adequate [44].

A total of 43.0% of patients were treated with unmodified cellulose, 12.6% with modified cellulose and 44.4% with synthetic dialyzers. Specifically, 92.7% of patients at the VAMC, 54.4% of patients at GWUMC, and 1.0% of patients at HUMC were treated with synthetic dialyzers, whereas 7.3% of patients at the VAMC, 30.4% of patients at GWUMC and 75.0% of patients at HUMC were treated with unmodified cellulose dialyzers. There was no difference between the mean age or the proportion of patients with diabetes mellitus treated with each type of dialyzer. Fewer women were treated with synthetic, and more were treated with unmodified cellulose dialyzers, in part because of the lower proportion of women treated at the VAMC. The mean serum albumin concentration was lower in patients treated with modified cellulose compared with unmodified cellulose and synthetic dialyzers (3.5 ± 0.43 vs. 3.8 ± 0.51, and 3.9 ± 0.43 g/dl, $P < 0.0001$, ANOVA). Mean Kt/V was significantly higher in patients treated with synthetic (1.3 ± 0.34), compared with unmodified (1.2 ± 0.27) or modified cellulose dialyzers (1.2 ± 0.31, $P < 0.006$, ANOVA). There was no difference between mean levels of age, BDI, CDI, SWLS, IEQ, MSPTOT, or behavioral compliance parameters in patients treated with different types of dialyzers.

Psychological and compliance data

The mean BDI score for the entire population was 11.4 ± 8.1, in the range of mild depression (Table 2) [30]. The mean MSPTOT score was 22.1 ± 4.5, which is similar to university student normative samples [45]. The patients' mean IEQ score was 64.4 ± 26.3, which is comparable to scores for a general medical inpatient sample, and samples of patients with arthritis and chronic pain [46]. The patients' mean SWLS score was 21.7 ± 7.9, which is comparable to normative adult samples [40]. Behavioral compliance data were available for 292 (99%) of the patients. The mean percent time compliance was 97.8 ± 2.9%, with a range of 83.3 to 100%. The mean percent attendance was 98.3 ± 6.1%, with a range of 38.8 to 100%, and the mean total time compliance was 95.9 ± 7.0%, with a range of 36.4 to 100%. These averages are comparable to those previously reported by others [47, 48].

Stability of psychosocial measures

Patients' individual baseline, six-monthly and one year social support, IEQ, SWLS, BDI and CDI scores correlated highly (r range 0.50 to 0.83, all $P < 0.001$), indicating high stability over time.

Correlations of medical, psychosocial and compliance data

Increased patient age was associated with an increased severity coefficient ($r = 0.94$, $P = 0.0001$), higher SWLS scores ($r = 0.27$, $P = 0.0001$), less shortening and skipping behavior and improved total time compliance ($r = 0.23$, $P = 0.0001$, $r = 0.17$, $P = 0.004$, $r = 0.27$, $P = 0.0001$, respectively), but with no other psychosocial variables (Table 3). Increased severity coefficient scores were associated with higher SWLS scores ($r = 0.22$, $P = 0.0001$), as seen in previous studies of patients with ESRD and in other populations [36], as well as less shortening and skipping behavior and improved total time compliance ($r = 0.18$, $P = 0.002$, $r = 0.16$, $P = 0.006$, $r = 0.23$, $P = 0.0001$, respectively). No psychosocial parameter correlated with serum albumin levels. The psychological and social variables tended to be highly intercorrelated (as previously reported [21, 36]; data not shown). Increased BDI and CDI scores, connoting worsened depression, correlated with

Table 3. Correlation matrix of selected medical and psychosocial factors

	BDI	MSP	IEQ	SWLS	SEV	S_{Alb}	%COMP	%ATTEND	%TCOMP
Age[a]	−0.05	0.03	0.004	0.27	0.94	−0.08	0.22	0.17	0.27
	0.40	0.67	0.95	0.0001	0.0001	0.16	0.0001	0.004	0.0001
SEV[b]	−0.02	−0.06	0.03	0.22	—	−0.09	0.18	0.16	0.23
	0.75	0.33	0.59	0.0001	—	0.13	0.002	0.006	0.0001
S_{Alb}	−0.06	−0.04	−0.03	−0.07	−0.09	—	−0.08	0.04	−0.03
	0.28	0.51	0.62	0.21	0.13	—	0.16	0.48	0.63
Kt/V	−0.02	−0.04	−0.07	0.04	0.09	−0.008	−0.04	0.04	−0.001
	0.72	0.49	0.29	0.52	0.14	0.16	0.55	0.47	0.98
%COMP	−0.08	−0.005	−0.07	0.07	0.18	−0.08	—	0.11	0.78
	0.13	0.93	0.24	0.21	0.002	0.17	—	0.05	0.0001
%ATTEND	−0.09	0.11	−0.12	0.16	0.16	0.04	0.11	—	0.63
	0.12	0.07	0.04	0.005	0.006	0.48	0.05	—	0.0001
%TCOMP	−0.12	0.04	−0.10	0.13	0.23	−0.03	0.78	0.11	—
	0.04	0.54	0.08	0.03	0.0001	0.63	0.0001	0.05	—

Abbreviations are: BDI, Beck Depression Inventory; MSP, Multidimensional Scale of Perceived Social Support, total score; IEQ, Illness Effects Questionnaire; SWLS, Satisfaction with Life Scale, total score; SEV, Severity Coefficient; S_{Alb}, Serum albumin concentration, *g/dl*; Kt/V, delivered dose of dialysis; %COMP, percent time on dialysis (inverse of shortening behavior); %ATTEND, percent attendance (inverse of skipping behavior); %TCOMP, total time compliance.

[a] r

[b] *P* value

Table 4. Predicting mortality from medical and demographic risk factors

Risk factors	RR (95% C.I.)	*P*
Age	1.65 (1.33, 2.04)	<0.0001
Severity coefficient	1.67 (1.37, 2.02)	<0.0001
Serum albumin concentration	0.76 (0.62, 0.93)	<0.01
Gender	1.00 (0.64, 1.55)	0.99
Kt/V (3 month mean)	0.95 (0.77, 1.18)	0.67
Dialyzer type	0.65 (0.43, 0.98)	0.04

Abbreviations are: RR, Risk Ratio; C.I., Confidence Interval. All variables are standardized to a standard deviation of 1.0, except for the two binary predictors (dialyzer and gender). Dialyzer types are detailed in the text.

worsened total time compliance ($r = -0.12$, $P = 0.04$, $r = -0.13$, $P = 0.026$, respectively) but not with shortening or skipping behavior. More negative IEQ scores (connoting increased perception of disruptive effects of illness) were associated with worsened attendance ($r = -0.12$, $P = 0.04$), but not with other behavioral compliance scores. Increased SWLS scores were associated with improved attendance and total behavioral compliance ($r = 0.16$, $P = 0.005$, $r = 0.13$, $P = 0.027$). MSPTOT scores did not correlate with any behavioral compliance measure.

Survival analyses

A Cox regression applied to the entire sample confirmed, as expected, a 40% increased mortality risk for each decade increase in age ($P < 0.0001$; data not shown). There was a 65% and 67% increased mortality risk for each one SD increase in age and severity coefficient, respectively ($P < 0.0001$, Table 4). There was a 24% decrease in mortality risk for each one SD increase in patients' serum albumin concentration ($P < 0.01$, Table 4), and a 50% decrease in risk for each 1 g/dl increase in albumin concentration, controlling for age and severity coefficient ($P < 0.01$, data not shown). No association was present between mortality risk and gender or level of Kt/V, with or without controlling for age and/or severity coefficient, in this comparatively small population.

There was no difference in the mean value of any assessed parameter between patients treated with unmodified cellulose dialyzers (Group 1) compared with those treated with modified cellulose and synthetic dialyzers (Group 2). The difference between the mean levels of Kt/V between patients treated with Group 1 and 2 dialyzers approached but did not reach the level of significance ($P = 0.0514$, unpaired *t*-test). There was no difference in the proportion of patients with diabetes mellitus treated with these two different categories of dialyzers, although a greater proportion of women were treated with unmodified cellulose dialyzers ($P = 0.001$, Chi square), and the proportion of patients treated with different types of dialyzers varied between the different study sites. Patients treated with modified cellulose and synthetic dialyzers had a 35% decreased mortality risk compared with those treated with unmodified cellulose dialyzers, with (data not shown) and without controlling for severity coefficient (both $P = 0.04$, Table 4).

Finally, the effects of variation in compliance and psychosocial parameters were tested. In each case, patients' age, severity coefficient, level of serum albumin concentration and dialyzer type were entered in the Cox regression first, and thus controlled for prior to testing for compliance and psychosocial effects. A one SD improvement in percent time compliance and total time compliance was associated with a 24% and 21% reduction in relative mortality risk (C.I. 0.62 to 0.91, 0.66 to 0.95, respectively, both $P < 0.01$, Table 5). The 13% decreased mortality risk associated with improved attendance at dialysis sessions did not, however, reach the level of statistical significance.

Table 5. Predicting mortality from compliance indicators and psychosocial factors

Risk factors	Adjusted RR (95% C.I.)	*P*
% Time compliance	0.76 (0.62, 0.91)	<0.0001
% Attendance	0.87 (0.72, 1.05)	0.15
% Total time compliance	0.79 (0.66, 0.95)	0.01
Beck Depression Inventory	1.05 (0.87, 1.27)	0.59
Cognitive Depression Index	1.03 (0.85, 1.26)	0.73
Illness Effects Questionnaire	1.23 (1.00, 1.51)	0.05
Social Support (MSP)	0.80 (0.65, 0.98)	0.03
Satisfaction with Life Scale	0.83 (0.66, 1.04)	0.10

Abbreviations are: RR, Risk Ratio; C.I., Confidence Interval. All variables are standardized to a standard deviation of 1.0, so that the RR represents the expected change in mortality risk associated with a one standard deviation change in the risk factor. All relative risks are controlled for variations in patients' age, severity coefficient, serum albumin concentration, and dialyzer type. Details are in the text.

There was no association between the level of either depression index and relative mortality risk. In contrast, a 1 SD increase in patients' perception of social support was associated with a 20% decrease in relative mortality risk, after controlling for age, severity of comorbid illness, level of serum albumin concentration and dialyzer type (C.I. 0.65 to 0.98, $P = 0.03$, Table 5). A 1 SD increase in IEQ score (denoting an increased patient perception of disruptive effects of illness) was associated with a 23% increase in relative mortality risk, controlling for age, severity of comorbid illness, level of serum albumin concentration and dialyzer type (C.I. 1.00 to 1.51, $P = 0.05$). There was a trend towards association of increased satisfaction with life scores with improved survival, but the level of statistical significance was not achieved.

Similar results were obtained when survival time for each patient was determined both by the number of days between first dialysis and the end of the study observation period, or date of death (data not shown). In general, these relationships persisted when controlled for site, with the exception of the association between dialyzer type and survival.

DISCUSSION

Medical factors and mortality

As expected, age and severity of illness were associated with mortality in our population. Serum albumin concentration, an indicator of nutritional status, was also related to improved survival, as noted by others [2–5]. Surprisingly, Kt/V was not associated with survival in this study. This may be due to our relatively small sample size, or because of its lesser relationship to patient survival [3]. Kt/V has been noted to be a correlate of survival, but only in very large samples with long follow-up times. In addition, Kt/V, as used clinically, may not provide an adequate description of the actual delivery of dialysis over time. A study performed only during 1/13 of treatments (or 2% of the time when the determination is performed quarterly), on a day when the patient knows post-dialytic chemistries will be ascertained, may only provide a "snapshot" of that particular treatment. Kt/V therefore may not correlate with the actual delivery of dialysis over time, which is dependent on the patient's adherence to the dialysis prescription. Indeed, this was the case in this study, where Kt/V did not correlate with measured behavioral compliance parameters.

In this prospective study, we confirm the findings of Hakim et al regarding the association of survival and dialyzer type [9]. While there was a trend to lower levels of Kt/V in patients treated with unmodfied cellulose dialyzers compared with those treated with modified cellulose and synthetic dialyzers, the difference between the values did not achieve the level of statistical significance. In addition, the only differences between groups of patients treated with various dialyzer types in all the assessed parameters were gender and site differences. To our surprise, however, in contrast to the other medical and psychosocial risk factors, the dialyzer effect was not significant when controlled for site. These findings suggest, besides clearance and the parameters suggested by Hakim et al, that specific site factors may be associated with the differential mortality seen in patients dialyzed with different dialyzers. This suggests that disparities in mortality are not necessarily related to characteristics of the membrane (and patient/membrane interactions), but may be due to physician or unit factors, including the manner in which the membranes are used, including water treatment protocols, which may ultimately be the proximate cause of variations in outcome [49]. Such notions must be assessed in carefully planned, multicenter, randomized, prospective controlled studies.

Psychosocial factors and mortality

Depression. We had hypothesized depression would be related to patients' poorer survival, potentially mediated through changes in compliance and nutrition. In this study, we could not demonstrate an association of depressive symptoms with survival, although depression was correlated with various psychosocial factors and with decreased behavioral compliance parameters. Thus, we were unable to replicate the previously reported association of depression and mortality [15]. The present results, however, are consistent with those of another study [16]. Additional research is needed regarding the relationship of depression and mortality, which may only hold with short-term predictions [14, 15], or in samples which include large numbers of very depressed patients.

Social support. Our study supports the hypothesis that social support is related to mortality among chronically ill patients, in particular among inner city African Americans. That social support can significantly add to the prediction of mortality when a large number of medical variables are controlled suggests its very robust effects. Our findings are consistent with the view that social support is an important factor in general health outcome and adjustment to chronic

and acute illness [10, 13, 16]. Indeed, lack of social support has been associated with increased mortality and morbidity in several studies from the U.S. and abroad, in populations with different chronic illnesses characterized by differing geographic settings, socioeconomic status and ethnic backgrounds [10]. High levels of social support have been associated with increased use of cancer screening services in older African-American patients [50]. Other studies have shown support from friends and others was independently related to survival in women with breast cancer [51, 52].

Associations between indicators of social support and survival have also been demonstrated in recent studies of patients with ESRD [16, 53–57]. McClellan and colleagues showed, in a prospective study, that a quality of life measure, which included social support, predicted survival of HD patients [53]. Christensen et al showed family cohesion, as a social support indicator, was significantly associated with survival, independent of age, in a study of 78 in-center hemodialysis patients [16]. In the latter study, standard compliance parameters such as level of predialysis serum potassium, phosphorus, or interdialytic weight gain [21, 22] were not associated with survival. In both these studies, however, the effects of other various potential medical risk factors, including nutritional status, delivery of dialysis and quantitative compliance with the dialysis regimen were not assessed. In a recent study, McClellan and colleagues showed patients' assessment of level of giving social support was related to improved survival in a cohort of patients with ESRD treated with HD [57]. The relationship of social support to other medical and psychosocial parameters, however, was not explored in that study [57].

Although the association between social support and improved survival of patients with chronic illness is consistent in varying populations, the mechanisms underlying the association are unknown [10, 58]. One study in HD patients suggested that family support was related to compliance, assessed by standard compliance measures [54]. Most previous studies, however, did not include longitudinal reappraisals of psychologic or compliance parameters. In this study, we have demonstrated the stability of psychosocial factors over a period of several months after patients' initial assessment. Additionally, we found social support was related to extent of depressive symptoms, perception of illness effects and satisfaction with life in this study. Patients with high levels of social support may have increased access to health care providers, dialysis facilities and overall better health care habits. Also, the tendency of people with higher social support to having better mood, less perceived disruption from their illness and a better perceived quality of life may affect medical and biochemical factors in unknown ways. Social support, however, was not related to behavioral compliance measures in this study.

Perception of illness. Patients' perceptions of the intrusiveness of their illness was also associated with their poorer survival in this study. Models of coping with chronic illness suggest perception of illness may be as or more important to adjustment and coping with illness than its medical severity [38, 59]. Consistent with previous findings, perceived illness effects were not associated with severity of illness in the present study. This finding is in agreement with reports that perception of illness effects may not only be an important predictor of outcome, but, as a coping mechanism, may be amenable to change [59]. Patients' perception of their well-being, an important component of quality of life [36, 60], is easily assessed and might form an important part of the medical evaluation. Indeed, a recent study suggests patients' perceptions of their physical functional capacity were predictive of survival [61].

Compliance. We have demonstrated a relationship between behavioral compliance with the dialysis prescription and survival, above and beyond the effect of medical risk factors. This is particularly important because behavioral compliance should contribute to increased levels of nutrition and Kt/V over time. Few studies have employed time of dialysis delivery compared with prescribed time as a measure of compliance [21, 22, 36, 47, 48]. This approach provides a clear behavioral measure of patient compliance, in contrast to standard compliance measures [19]. We have previously shown behavioral compliance measures are, on the whole, largely unrelated to standard compliance measures [21, 22, 36]. Such findings suggest compliance in HD patients is comprised of several aspects, such as dietary behaviors, compliance with prescribed medication regimens and behavioral components, such as attendance at dialysis sessions. We have also previously demonstrated, in this study population, that patients' adherence to the dialysis prescription is stable, consistent, and typifies an individual subject over an extended time period [21].

In the present study, with a longer observation period, we have now demonstrated that psychosocial factors tend to remain stable in patients over one year. However, perception of social support from family, friends and others was not associated with patients' illness severity, or extent of behavioral compliance. In contrast, perception of illness intrusiveness was variably associated with several behavioral compliance measures. These findings are inconsistent with the idea that more severe medical illness leads to lower levels of perceived social support and decreased perception of well-being. They do support the notion that perception of well-being may exert its effects on survival through changes in compliance with the dialysis prescription.

Alternatively, the effects of perceptual variables and social support may be mediated through altered nutrition, or by affecting the psychoneuroimmunologic system [14, 59, 62], perhaps by reducing the effects of stress. Previous studies have suggested an interrelationship between psychological status, immune dysfunction, nutrition and outcome [14, 59, 62] However, patients' MSPTOT scores were not related to nutritional factors such as level of serum

albumin, mean upper arm circumference, or arm muscle area, standard anthropometric measures of malnutrition in this population [5, 43].

We could not demonstrate a relationship between behavioral compliance and Kt/V, the measure of the delivered dose of dialysis. Indeed, Kt/V represents the delivered dose of dialysis only if the patient complies with the prescription each and every treatment. Since psychosocial and well-being indices, and Kt/V were unrelated to measures of behavioral time compliance, it appears that this measure of adherence to the dialysis prescription, which is related to survival, may be both an important characteristic that may typify a patient [21], and an independent mechanism that influences mortality.

In this study, perception of extent of social support, level of well-being and improved behavioral compliance were associated with changes in the relative risk of mortality in the range of the magnitude of effects that age, severity of comorbid illness and serum albumin displayed [42]. Many medical risk factors are not easily altered in patients with ESRD. Although behavioral compliance with the dialysis prescription was associated with improved survival, we could not demonstrate an association of these parameters with Kt/V, the measured "dose" of dialysis. While improved behavioral compliance with the dialysis prescription will undoubtedly be associated with increased delivery of dialysis, our study may not have had enough power to detect such variations. Alternatively, compliance styles may reflect personality traits or social factors associated with improved survival. Our population had a relatively high Kt/V [44] and adequate nutritional status [43]. The effect of increasing dose of dialysis may be only appreciated in relatively large populations with longer follow-up. Additionally, there may be diminished returns of increasing delivery of dialysis when the Kt/V is already relatively high. Such questions are currently being addressed in prospective studies. However, differing psychosocial, perceptual and well being, and compliance factors, rather than medical or dialytic ones may be associated with the differential survival in patients in other countries that is currently of concern to national health policy makers [23].

Our study population was primarily comprised of male, African American, urban patients. In previous work, we demonstrated the relationship of psychosocial variables to behavioral compliance may be different in dialysis units with different patient populations, including those with differing gender composition, type of hemodialysis administered and dialyzers used, and mean prescribed dialysis time [21]. The present association of improved social support and perception of well-being with improved survival does not necessarily imply causality. Although MSPTOT and IEQ levels were not correlated with medical severity, other unknown mediating factors may be associated with both level of social support and perception of well-being and medical factors that affect outcome.

Our findings, while consistent with those documented in ESRD patients and those with other chronic diseases, must be replicated in larger and more diverse populations to establish the generalizable and specific outcomes reported. Another way to demonstrate causality would be to document the effect of a psychosocial intervention on survival in a population at risk. The first 25 years of the ESRD program were largely devoted to identifying and minimizing the medical risk factors associated with poor patient survival. The next step is to modify factors, such as perceptions of illness, level of social support and extent of behavioral compliance with the dialysis prescription, which are remediable or are under the patients' control, in an attempt to improve both their quality and length of life. We should listen to our patients' perceptions of how their ESRD variably affects their lives—they may be telling us about their mortality risk. We should continue our efforts to encourage both patient compliance with the dialysis prescription and with dietary regimens. The effect of interventions to increase behavioral and dietary compliance with the dialysis prescription, social support, and perceptions of well-being, and their effect on survival in hemodialysis patients should be studied further.

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APPENDIX

Abbreviations used in this article are: AMA, arm muscle area; %ATTEND, percent attendance; BDI, Beck Depression Inventory; CDI, Cognitive Depression Index; %COMP, percent time compliance; ESRD, end-stage renal disease; GWUMC, George Washington University Medical Center; HD, hemodialysis; HUMC, Howard University Medical Center; IEQ, Illness Effects Questionnaire; Kt/V, delivery of dialysis; MAC, mid-arm circumference; MSP, Multidimensional Scale of Perceived Social Support; MSPTOT, total social support score; PCR, protein catabolism rate; SWLS, Satisfaction with Life Scale; VAMC, Veteran's Administration Medical Center.

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